

1060 1070 1080 1090 1100 1110 1120

ATACCAGGAC ATTGTATGAC GTTCCCTGCT CACATGCCTG CTTTCTTCCT ATAATACAGA TGCTCAACTA

1130 1140 1150 1160 1170 1180 1190

ACTGCTCATG TCCTTATATC ACAGAGGGAA ATTGGAGCTA TCTGAGGAAC TGCCCAGAAG GGAAGGGCAG

1200 1210 1220 1230 1240 1250 1260

AGGGGTCTTG CTCTCCTTGT CTGAGGCCATA ACTCTTCTTT CTACCTTCCA GTGAACACCT TCCCACCCCCA

1270 1280 1290 1300 1310 1320 1330

GGTCCACCTG CTACCGCCGC CGTCGGAGGA GCTGGCCCTG AATGAGCTCT TGTCCCTGAC ATGCCCTGGTG

1340 1350 1360 1370 1380 1390 1400

CGAGCTTTCA ACCCTAAAGA AGTGCTGGTG CGATGGCTGC ATGGAAATGA GGAGCTGTCC CCAGAAAGCT

1410 1420 1430 1440 1450 1460 1470

ACCTAGTGTG TGAGCCCCTA AAGGAGCCAG GCGAGGGAGC CACCACCTAC CTGGTGACAA GGTGTTGCG

1480 1490 1500 1510 1520 1530 1540

TGTATCAGCT GAAAGCTTGA TATCGAATTC CGGAGGGGAA ACCGGCAGTG CAGCCCGAAG CCCCGCAGTC

1550 1560 1570 1580 1590

CCCGAGCAGC CGTGGCC ATG CGT CCC CTG CGC CCC CGC GCC GCG CTG CTG GCG CTC CTG
Met Arg Pro Leu Arg Pro Arg Ala Ala Leu Leu Ala Leu Leu>
____a____a____a____a____a____ORF RF[1] ____a____a____a____a____a____>

1600 1610 1620 1630 1640 1650

GCC TCG CTC CTG GCC GCG CCC CCG GTG GCC CCG GCC GAG GCC CCG CAC CTG GTG CAT
Ala Ser Leu Leu Ala Ala Pro Pro Val Ala Pro Ala Glu Ala Pro Eis Leu Val His>
____a____a____a____a____a____a____ORF RF[1] ____a____a____a____a____a____a____>

1660 1670 1680 1690 1700 1710

GTG GAC GCG GCC CGC GCG CTG TGG CCC CTG CGG CGC TTC TGG AGG AGC ACA GGC TTC
Val Asp Ala Ala Arg Ala Leu Trp Pro Leu Arg Arg Phe Trp Arg Ser Thr Gly Phe>
____a____a____a____a____a____a____ORF RF[1] ____a____a____a____a____a____a____>

1720 1730 1740 1750 1760 1770

TGC CCC CCG CTG CCA CAC AGC CAG GCT GAC CAG TAC GTC CTC AGC TGG GAC CAG CAG
Cys Pro Pro Leu Pro His Ser Gln Ala Asp Gln Tyr Val Leu Ser Trp Asp Gln Gln>
____a____a____a____a____a____a____ORF RF[1] ____a____a____a____a____a____a____>

1780 1790 1800 1810 1820

CTC AAC CTC GCC TAT GTG GGC GCC GTC CCT CAC CGC GGC ATC AAG CAG GTC CGG ACC
Leu Asn Leu Ala Tyr Val Gly Ala Val Pro His Arg Gly Ile Lys Gln Val Arg Thr>
____a____a____a____a____a____a____ORF RF[1] ____a____a____a____a____a____a____>

1830 1840 1850 1860 1870 1880

CAC TGG CTG CTG GAG CTT GTC ACC ACC AGG GGG TCC ACT GGA CGG GGC CTG AGC TAC
His Trp Leu Leu Glu Leu Val Thr Thr Arg Gly Ser Thr Gly Arg Gly Leu Ser Tyr>

FIGURE 1B

3090 3100 3110 3120 3130

3140 3150 3160 3170 3180 3190

3200 **3210** **3220** **3230** **3240** **3250**

... 3260 3270 3280 3290 3300

3310 **3320** **3330** **3340** **3350** **3360**

3370 **3380** **3390** **3400** **3410** **3420**

3430 3440 3450 3460 3470 3480

3490 3500 3510 3520 3530 3540

3550 * 3560 * 3570 * 3580 * 3590 * 3600 * 3610 *
 CTTGCCACCTC CACCGGGCAGT CAGCGAGCTG GGGCTGCACT GTGCCCATGC TGCCCTCCCA TCACCCCCCTT

3620 3630 3640 3650 3660 3670 3680

3890 3900 3910 3920 3930 3940 3950 3960 3970 3980 3990 4000

FIGURE 1D

AAAAAAAAAA AAAAAAAAAG AATTCTGCA GCCCGGGGGA TCCACTAGTT CTAGAGGGCC CGTTAAACC
 3760 3770 3780 3790 3800 3810 3820
 CGCTGATCAG CCTCGACTGT GCCTCTAGT TGCCAGCCAT CTGTTGTTG CCCCTCCCCC GTGCCTTCCT
 3830 3840 3850 3860 3870 3880 3890
 TGACCCCTGGA AGGTGCCACT CCCACTGTCC TTTCTAATA AAATGAGGAA ATTGCATCGC ATTGTCTGAG
 3900 3910 3920 3930 3940 3950 3960
 TAGGTGTCAT TCTATTCTGG GGGGTGGGT GGGGCAGGAC AGCAAGGGG AGGATTGGGA AGACAATAGC
 3970 3980 3990 4000 4010 4020 4030
 AGGCATGCTG GGGATGCGGT GGGCTCTATG GCTTCTGAGG CGGAAGAAC CAGCTGGGC TCGAGAGCTT
 4040 4050 4060 4070 4080 4090 4100
 GGCGTAATCA TGGTCATAGC TGTTTCTGT GTGAAATTGT TATCCGCTCA CAATTCCACA CAACATACGA
 4110 4120 4130 4140 4150 4160 4170
 GCCGGAAGCA TAAAGTGTAA AGCCTGGGT GCCTAATGAG TGAGCTAACT CACATTAAATT GCGTTGCGCT
 4180 4190 4200 4210 4220 4230 4240
 CACTGCCCGC TTTCCAGTCG GGAAACCTGT CGTGCAGCT GCATTAATGA ATCGGCCAAC GCGCGGGGAG
 4250 4260 4270 4280 4290 4300 4310
 AGGCGGTTTG CGTATTGGGC GCTCTCCGC TTCCTCGCTC ACTGACTCGC TGCGCTCGGT CGTCGGCTG
 4320 4330 4340 4350 4360 4370 4380
 CGGGGAGCGG TATCAGCTCA CTCAAAGCG GTAAATACGGT TATCCACAGA ATCAGGGGAT AACGCAAGAA
 4390 4400 4410 4420 4430 4440 4450
 AGAACATGTG AGCAAAAGGC CAGCAAAAGG CCAGGAACCG TAAAAAGGCC GCGTTGCTGG CGTTTTCCA
 4460 4470 4480 4490 4500 4510 4520
 TAGGCTCCGC CCCCTGACG AGCATCACAA AAATGACGC TCAAGTCAGA GGTGGCGAAA CCCGACAGGA
 4530 4540 4550 4560 4570 4580 4590
 CTATAAAGAT ACCAGGCGTT TCCCCCTGGA AGCTCCCTCG TGCGCTCTCC TGTTCCGACC CTGCCGCTTA
 4600 4610 4620 4630 4640 4650 4660
 CCGGATACCT GTCCGCCTTT CTCCCTTCGG GAGCGTGGC GCTTCTCAA TGTCACCGCT TAGGTATCT
 4670 4680 4690 4700 4710 4720 4730
 CAGTTGGTG TAGTCGTTG GCTCCAAGCT GGGCTGTGTG CACGAACCCC CCGTTCAAGCC CGACCGCTGC
 4740 4750 4760 4770 4780 4790 4800
 GCCTTATCCG GTAACTATCG TCTTGAGTCC AACCCGGTAA GACACGACTT ATCGCCACTG GCAGCAGCCA

FIGURE 1E

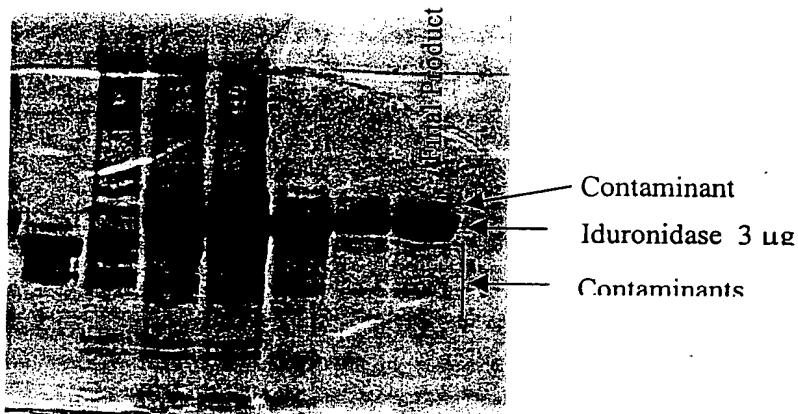
4810	4820	4830	4840	4850	4860	4870
*	*	*	*	*	*	*
CTGGTAACAG GATTAGCAGA GCGAGGTATG TAGGCGGTGC TACAGAGTTC TTGAAGTGGT GGCCTAACTA						
4880	4890	4900	4910	4920	4930	4940
*	*	*	*	*	*	*
CGGCTACACT AGAAGGACAG TATTTGGTAT CTGCGCTCTG CTGAAGCCAG TTACCTTCGG AAAAAGAGTT						
4950	4960	4970	4980	4990	5000	5010
*	*	*	*	*	*	*
GGTAGCTCTT GATCCGGCAA ACAAAACCACC GCTGGTAGCG GTGGTTTTT TGTGACGCAAG CAGCAGATTA						
5020	5030	5040	5050	5060	5070	5080
*	*	*	*	*	*	*
CGCGCAGAAA AAAAGGATCT CAAGAAGATC CTTTGATCTT TTCTACGGGG TCTGACGCTC AGTGGAACGA						
5090	5100	5110	5120	5130	5140	5150
*	*	*	*	*	*	*
AAACTCACGT TAAGGGATTG TGGTCATGAG ATTATCAAAA AGGATCTTCA CCTAGATCCT TTTAAATTAA						
5160	5170	5180	5190	5200	5210	5220
*	*	*	*	*	*	*
AAATGAAGTT TTAAATCAAT CTAAAGTATA TATGAGTAA CTTGGTCTGA CAGTTACCAA TGCTTAATCA						
5230	5240	5250	5260	5270	5280	5290
*	*	*	*	*	*	*
GTGAGGCACC TATCTCAGCG ATCTGTCTAT TTCTGTCATC CATAAGTGCC TGACTCCCCG TCGTGTAGAT						
5300	5310	5320	5330	5340	5350	5360
*	*	*	*	*	*	*
AACTACGATA CGGGAGGGCT TACCATCTGG CCCCCAGTGCT GCAATGATAAC CGCGAGACCC ACGCTCACCG						
5370	5380	5390	5400	5410	5420	5430
*	*	*	*	*	*	*
GCTCCAGATT TATCAGCAAT AAACCAAGCCA GCCGGAAGGG CCGAGGCCAG AAGTGGTCCT GCAACTTTAT						
5440	5450	5460	5470	5480	5490	5500
*	*	*	*	*	*	*
CCGCCTCCAT CCAGTCTATT AATTGTTGCC GGGAAAGCTAG AGTAAGTGTAGT TCGCCAGTTA ATAGTTTGC						
5510	5520	5530	5540	5550	5560	5570
*	*	*	*	*	*	*
CAACGTTGTT GCCATTGCTA CAGGCATCGT GGTGTCACCGC TCGTCGTTTG GTATGGCTTC ATTCAAGCTCC						
5580	5590	5600	5610	5620	5630	5640
*	*	*	*	*	*	*
GGTTCCCAAC GATCAAGGGG AGTTACATGA TCCCCCATGT TGTGAAAAA AGCGGTTAGC TCCTTCGGTC						
5650	5660	5670	5680	5690	5700	5710
*	*	*	*	*	*	*
CTCCGATCGT TGTCAAGAAGT AAGTTGGCCG CAGTGTATC ACTCATGGTT ATGGCAGCAC TGCATAATTTC						
5720	5730	5740	5750	5760	5770	5780
*	*	*	*	*	*	*
TCTTACTGTC ATGCCATCCG TAAGATGCTT TTCTGTGACT GGTGAGTACT CAACCAAGTC ATTCTGAGAA						
5790	5800	5810	5820	5830	5840	5850
*	*	*	*	*	*	*
TAGTGTATGC GGCAGCCGAG TTGCTCTTGC CCGGGGTCAA TACGGGATAA TACCGCGCCA CATGGCAGAA						
5860	5870	5880	5890	5900	5910	5920
*	*	*	*	*	*	*

Digitized by srujanika@gmail.com

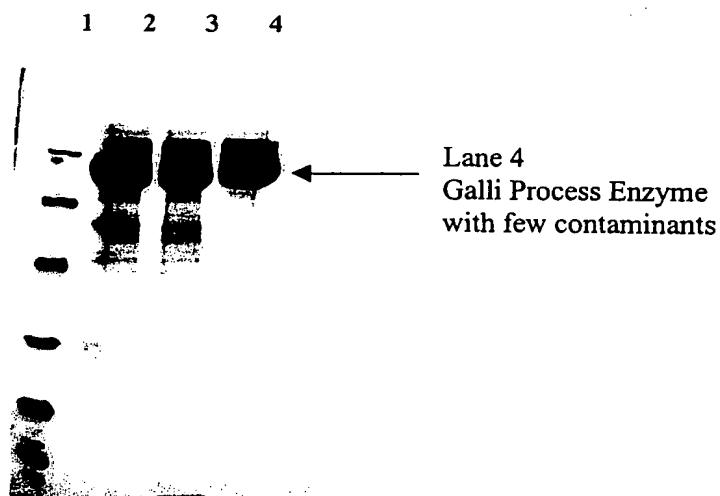
FIGURE 1G

FIGURE 2. SDS-POLYACRYLAMIDE GELS DEMONSTRATING IMPROVEMENTS IN PURITY

Gel using the Kakkis et al 1994, published procedure for purification



Gel using the new Galli Process contained in this application



1. Molecular Weight Marker
2. Prior Process Carson (nonpublished) Batch 2000C9001 Reference Reduced (7.5 μ g)
3. Same Batch 2000C9001 Reference Reduced (5.0 μ g)
4. Galli Process Enzyme Batch P10006 (5.0 μ g)

FIGURE 2

FIGURE 3A IDURONIDASE PRODUCTION USING THE GALLI PROCESS

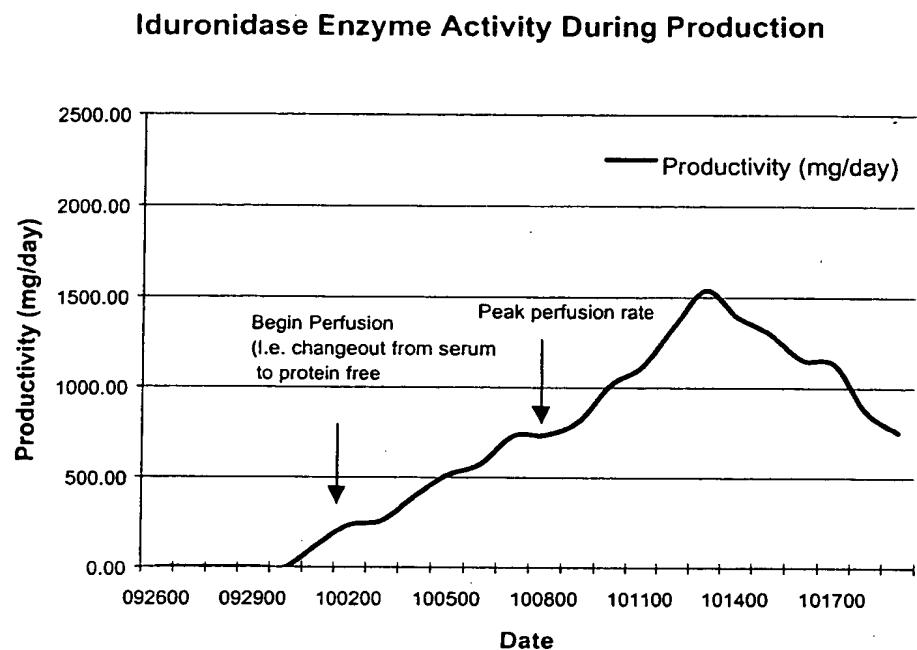
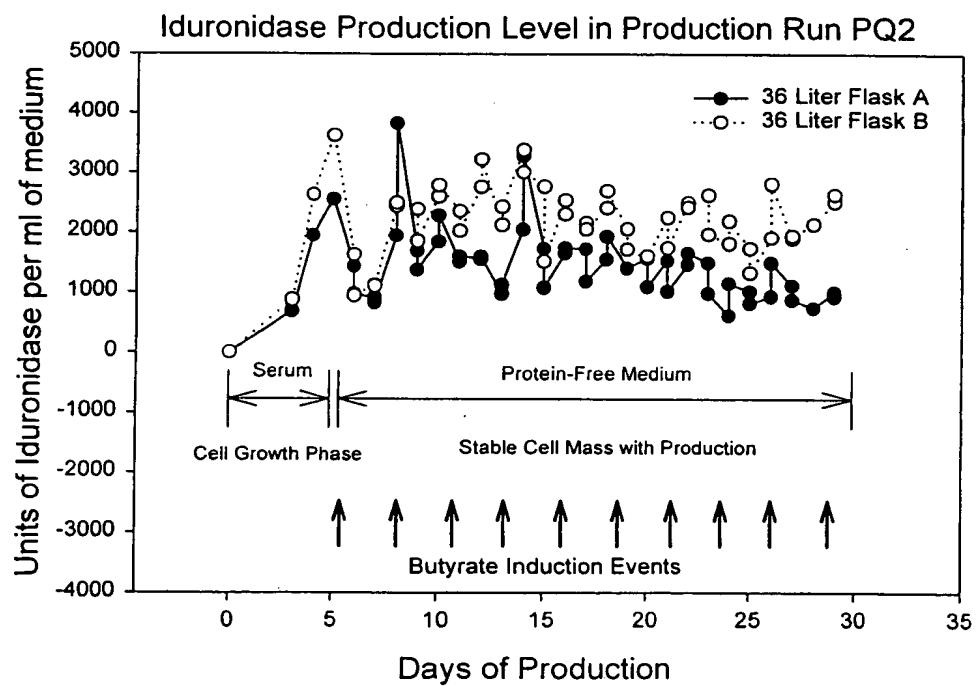


FIGURE 3B. IDURONIDASE PRODUCTION USING BUTYRATE INDUCTION



Reduction in Liver Volume During Enzyme Therapy

FIGURE 4

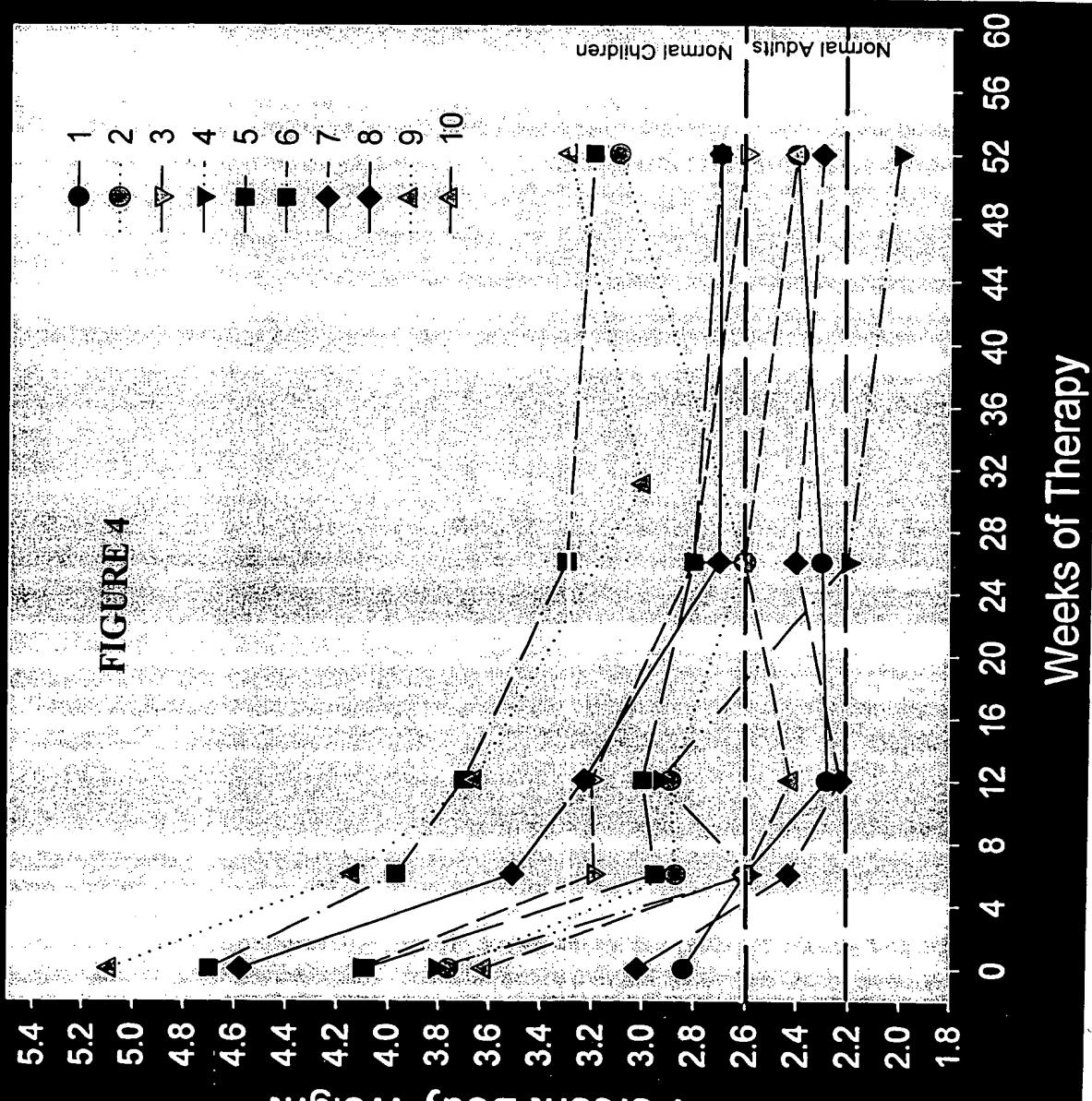


FIGURE 4

Urinary GAG Excretion During Enzyme Therapy

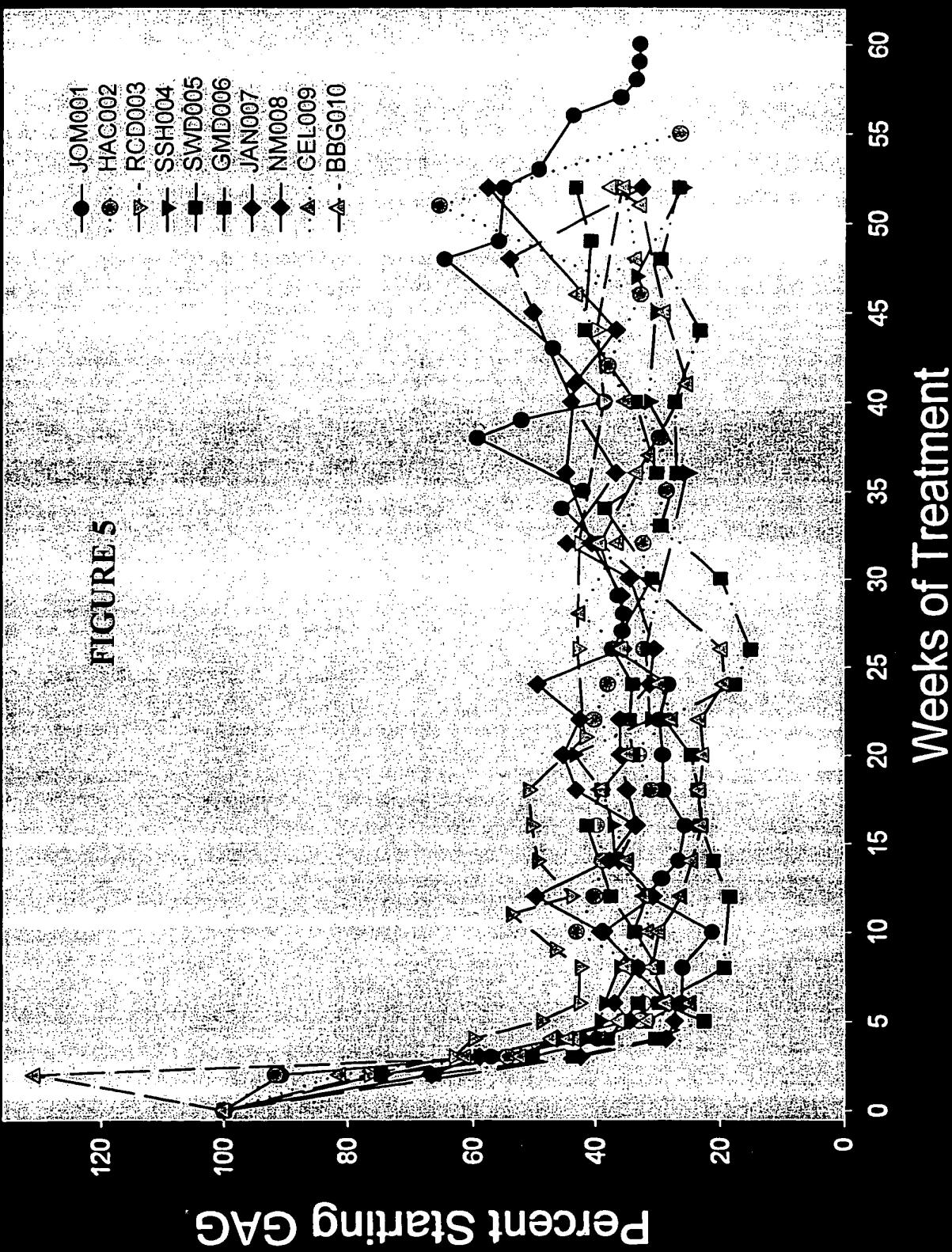


FIGURE 5

Elbow and Knee Extension in HAC002

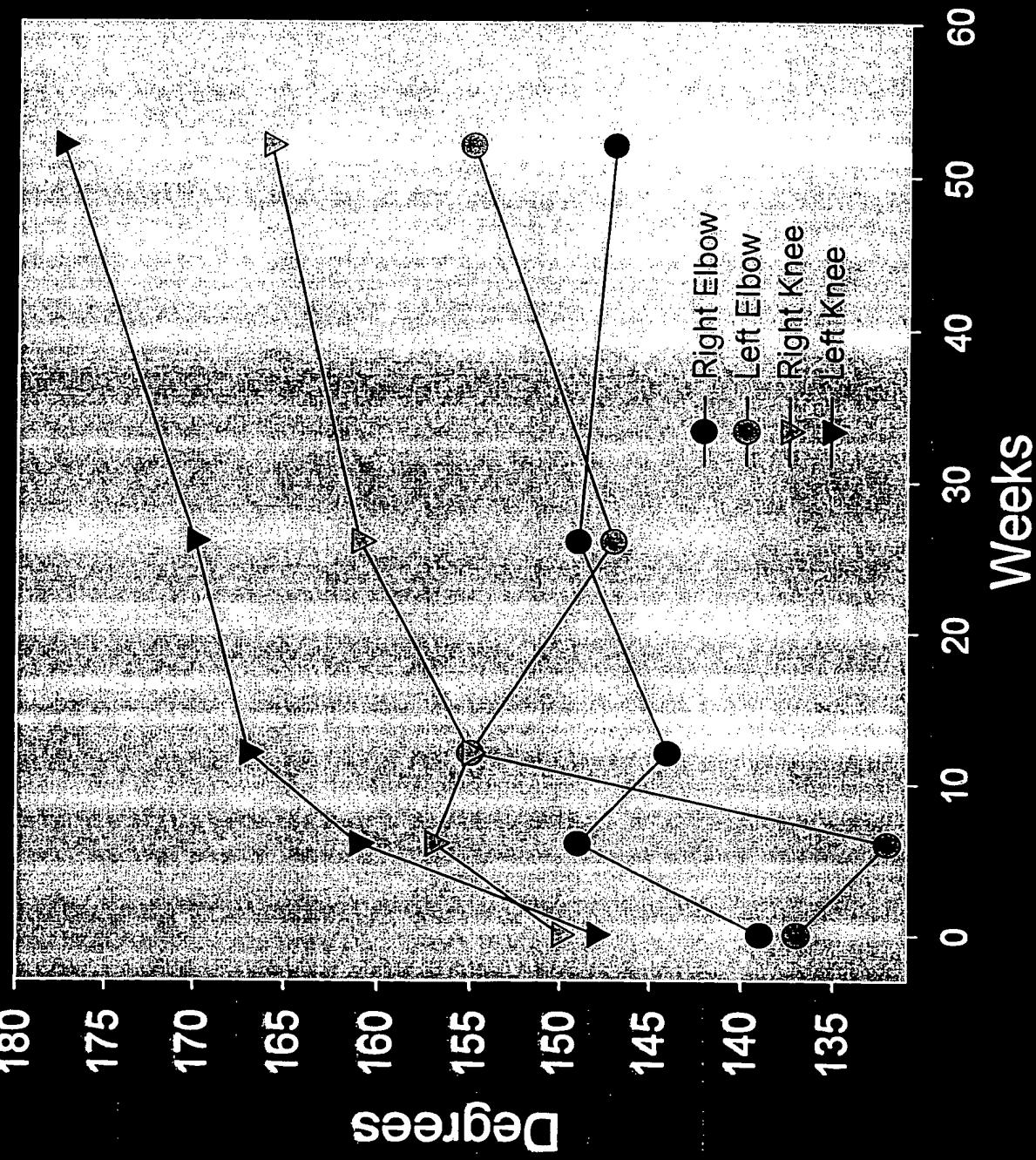


FIGURE 6

Shoulder flexion to 104 weeks in four patients with most restriction

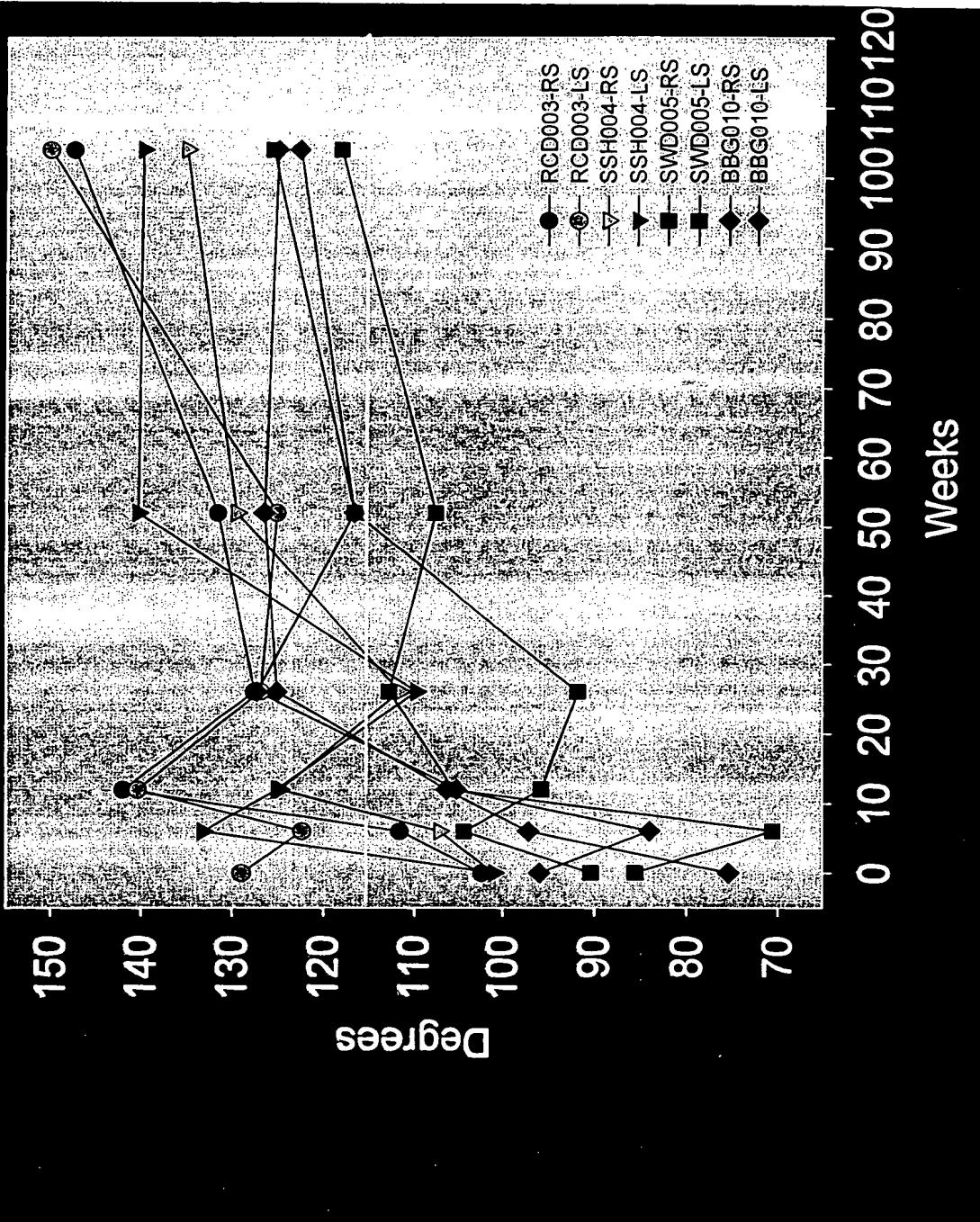


FIGURE 7

Sleep Apnea Improves

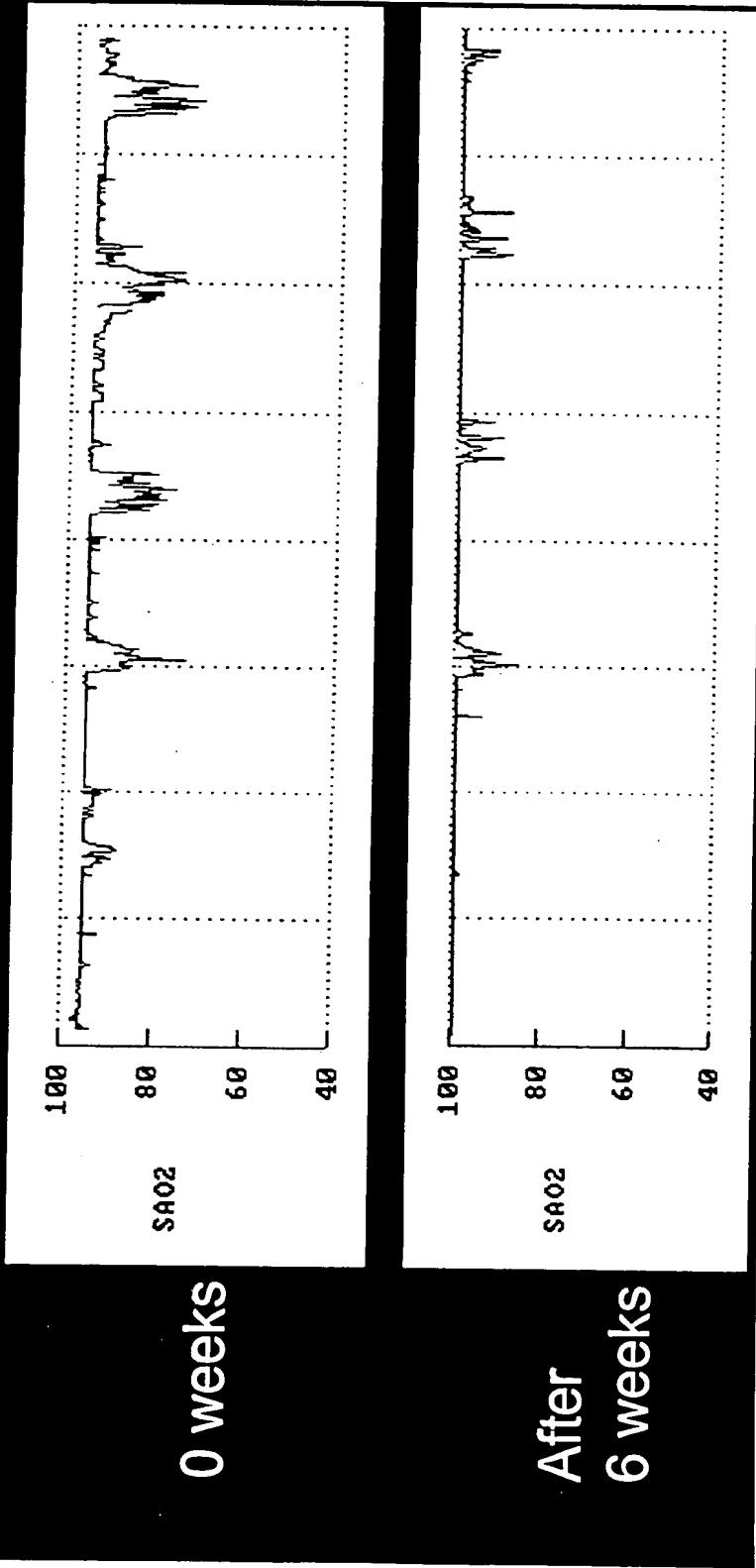


FIGURE 8

200207142005

Apneas + Hypopneas During Sleep Pre and Post Treatment

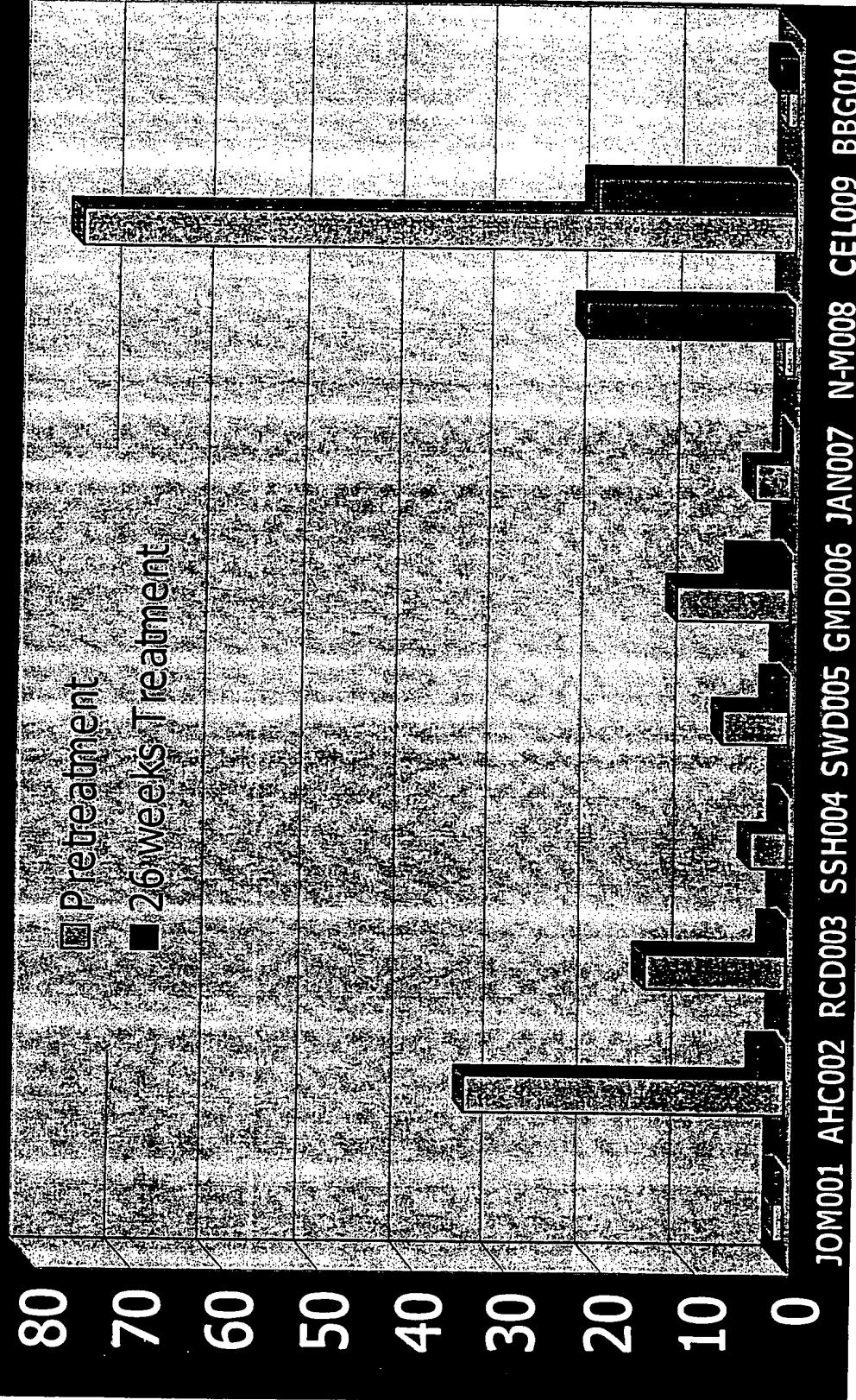


FIGURE 9

JOM001 AHC002 RCD003 SSH004 SWD005 GMD006 JAN007 N-M008 CEL009 BBG010

Pulmonary Function Tests in GMD006

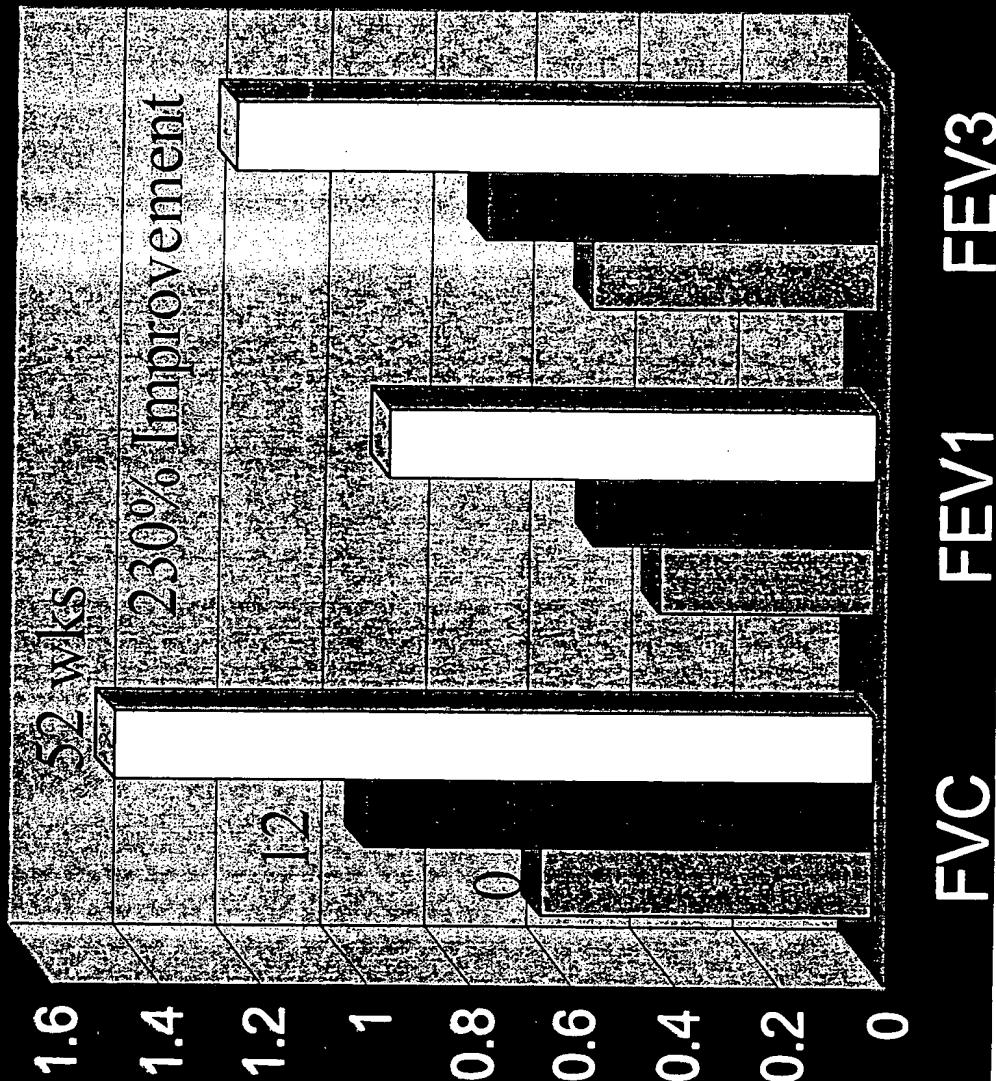


FIGURE 10

Increased Height Growth Velocity

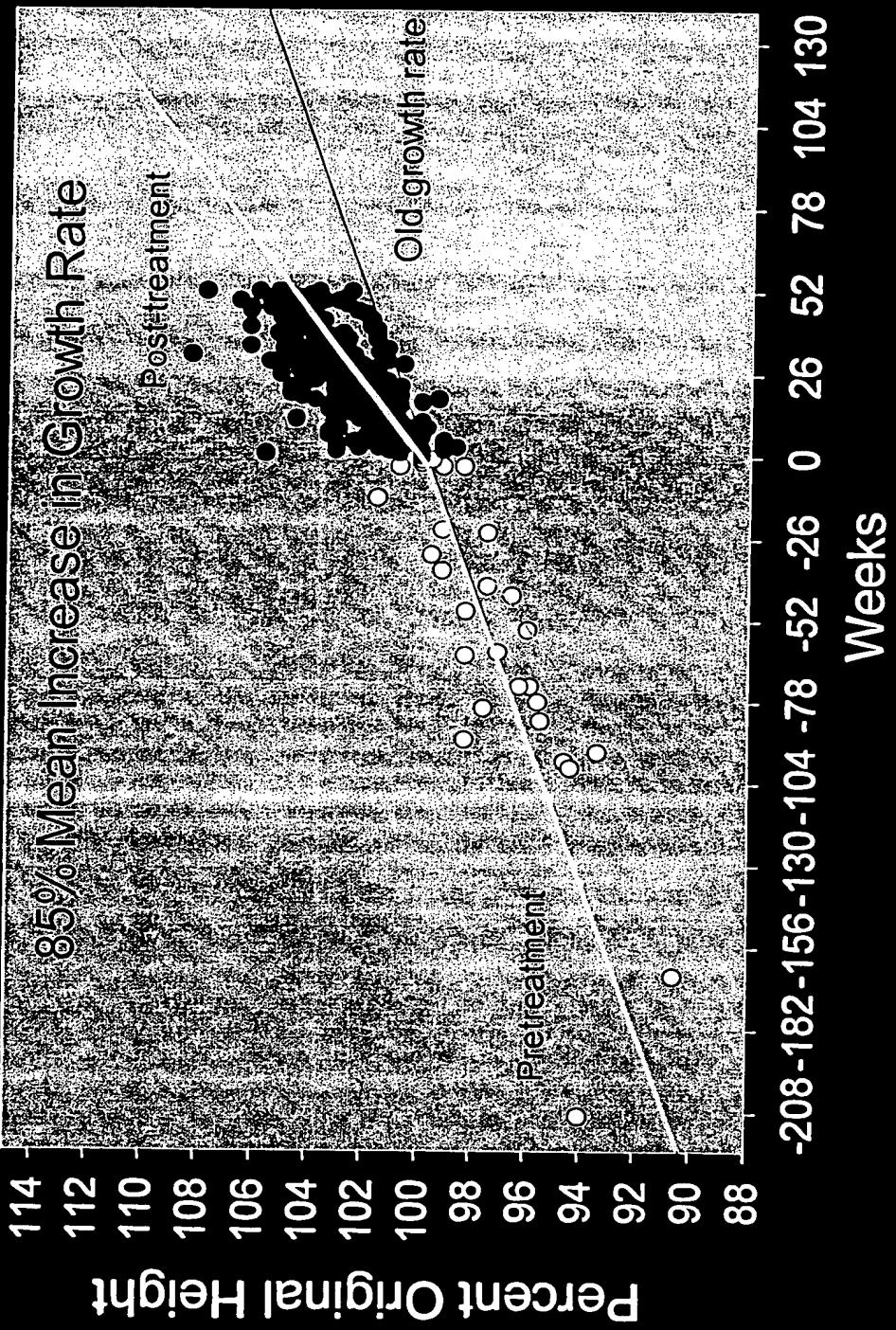


FIGURE 11

FIGURE 12.

COMPARISON OF HOST PROTEIN CONTAMINATION BETWEEN A PRIOR AND THE NEW GALLI PROCESS

Chinese Hamster Ovary Host Protein Contamination by ELISA Assay

Source and Batch Number	Chop Protein Contamination (microgram per milligram)	Percent Chop Contamination	Purity of the Enzyme from Chop
Prior Process (Carson/REI)			
C9002	14	1.4%	98.6%
C9003	24	2.4%	97.6%
C9004	16	1.6%	98.4%
New Process (Galli)			
P1003	<1.3	<0.13%	>99.9%
P1006	1.2	0.12%	99.9%
P1007	<0.6	<0.06%	>99.9%
P1008	<0.67	<0.067%	>99.9%

卷之三

FIGURE 12

Comparison of Galli and Carson Material

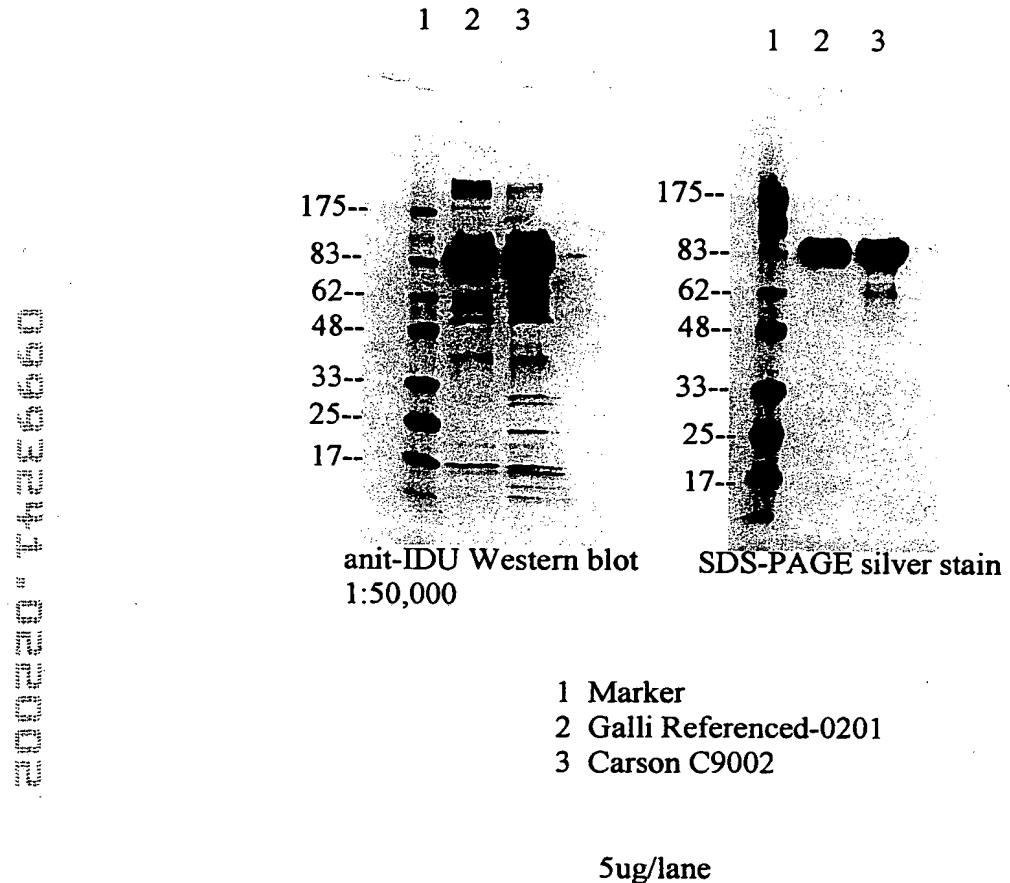


FIGURE 13